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L34 ANSWER 1 OF 17 MEDLINE
AN 1999086764 MEDLINE
DN 99086764 PubMed ID: 9869940
TI Experience with **pancreas islets** separation,
immunoisolation and cryopreservation.
AU Orłowski T; Tatarkiewicz K; Sitarek E; Sabat M; Fiedor P; Samsel R
CS Transplantation Institute, Warsaw Medical School, Poland.
SO ANNALS OF TRANSPLANTATION, (1996) 1 (1) 54-8.
Journal code: 9802544. ISSN: 1425-9524.
CY Poland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990119
AB Experience of Warsaw **Pancreas** Laboratory is presented. Some improvement in the methods of rat, human and pig **pancreases** digestion, and in identification of **Langerhans islets** by means of intravenous injection of I-DTZ was achieved. For immunoisolation of **islets**, 2 methods were elaborated: capsules containing alginate/polyethyleneimine/protamine/**heparin** membrane prepared by modified Sun method, and microcapsules based on Zekorn method. Biocompatibility of hollow fibers, prepared with polypropylene (PP), surface modified PP (PPS) and polysulphone (PS) was assessed in vitro. Only PS fibers were fully compatible. It was shown, that the mixture of exocrine tissue did not influence in vitro insulin secretion, providing that alginate in which **islets** are embedded remain gelled. The efficacy of 3 methods of **islets** cryopreservation was compared: freezing in "semicontrollable" conditions, in programmable Kriomedpol machine, and vitrification. The highest percentage of frozen/thawed living cells, and the most reliable results were obtained with Kriomedpol method.

CT Check Tags: Animal; Human
 Alginates
 Biocompatible Materials
 Capsules
 Cell Culture: MT, methods
 Cell Separation: MT, methods
 Cells, Cultured
 *Cryopreservation: MT, methods
 *Diabetes Mellitus, Experimental: SU, surgery
Heparin
 Indicators and Reagents
 Insulin: SE, secretion
***Islets of Langerhans**
 Islets of Langerhans: CY, cytology
 Islets of Langerhans: SE, secretion
 Mice
 Polyethyleneimine
 Polymers
 Polypropylenes
 Protamines
 Rats
 Sulfones
 Swine
 Time Factors
Transplantation, Heterologous

RN 11061-68-0 (Insulin); 25135-51-7 (polysulfone P 1700); 9002-98-6
 (Polyethyleneimine); 9005-32-7 (alginic acid); **9005-49-6 (Heparin)**

CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Capsules); 0 (Indicators
 and Reagents); 0 (Polymers); 0 (Polypropylenes); 0 (Protamines); 0
 (Sulfones)

L34 ANSWER 2 OF 17 MEDLINE
 AN **1998165631** MEDLINE
 DN **98165631** PubMed ID: **9506786**
 TI Comparison of two methods of **pancreas islets**
 immunoisolation.
 AU Orlowski T; Sitarek E; Tatarkiewicz K; Sabat M; Antosiak M
 CS Transplantation Institute, Warsaw School of Medicine, Warszawa, Poland.
 SO INTERNATIONAL JOURNAL OF ARTIFICIAL ORGANS, (1997 Dec) 20 (12)
 701-3.
 Journal code: 7802649. ISSN: 0391-3988.
 CY Italy
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199805
 ED Entered STN: 19980520
 Last Updated on STN: 19990129
 Entered Medline: 19980514

AB The efficacy of two methods of **Langerhans islets**
 immunoisolation was compared. For this purpose the function of
islets encapsulated with alginate/polyethylenimine/protamine/
heparin (APPH) or with alginate/poly-L-lisine/alginate (APA)
 membranes was assessed: in vitro according to their survival and response
 to glucose challenges, and in vivo according to their capability to
 provide sufficient insulin delivery to maintain normal fasting blood
 glucose following xenotransplantation to streptozotocin diabetic mice. In
 vitro insulin secretion and the response to glucose challenge of APPH and
 APA encapsulated **islets** were comparable to free **islets**
 . In vivo intraperitoneal concordant xenotransplantation of APA
 encapsulated rat **islets** reversed the diabetic state of
 streptozotocin diabetic mice for a longer period, than APPH **islet**
 grafts. This study clearly demonstrated the inadequacy of in vitro methods

in the prediction of in vivo results of **islets** transplantation.

CT Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
Alginates

Biocompatible Materials

Blood Glucose: AN, analysis

Diabetes Mellitus, Experimental: BL, blood

Diabetes Mellitus, Experimental: SU, surgery

*Diabetes Mellitus, Experimental: TH, therapy

Glucose: DU, diagnostic use

Insulin: SE, secretion

Islets of Langerhans: SE, secretion

Islets of Langerhans Transplantation: IM, immunology

***Islets of Langerhans Transplantation: MT, methods**

*Membranes, Artificial

Mice

Mice, Inbred BALB C

Pancreas, Artificial

Polylysine: AA, analogs & derivatives

Rats

Tissue Culture

Transplantation, Heterologous

RN 11061-68-0 (Insulin); 25104-18-1 (Polylysine); 50-99-7 (Glucose)

CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Blood Glucose); 0
(alginate-polylysine-alginate)

L34 ANSWER 3 OF 17 MEDLINE

AN **97438103** MEDLINE

DN **97438103** PubMed ID: **9293878**

TI Expansion of intermediate T cell receptor cells expressing interleukin-2
receptor alpha- beta+, CD8alpha+ beta+, and lymphocyte function-associated
antigen-1+ in the liver in association with intrahepatic islet xenograft
rejection from rat to mouse: prevention of rejection with
anti-interleukin-2 receptor beta **monoclonal antibody**
treatment.

AU Ohtsuka K; Yasunami Y; Ikehara Y; Nagai T; Kodama S; Maki T; Tomita A; Abo
T; Ikeda S

CS Department of Surgery I, Fukuoka University School of Medicine, Japan.

SO TRANSPLANTATION, (1997 Aug 27) 64 (4) 633-9.

Journal code: 0132144. ISSN: 0041-1337.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199709

ED Entered STN: 19971013

Last Updated on STN: 19971013

Entered Medline: 19970930

AB BACKGROUND: The precise mechanisms involved in islet xenograft rejection
remain unknown. The purpose of the present study was to determine cellular
mechanisms responsible for islet xenograft rejection in the liver to
facilitate finding a procedure for prevention of immune rejection.
METHODS: Hepatic mononuclear cells (MNC) as well as splenocytes,
peripheral blood MNC, and thymocytes from streptozotocin-induced diabetic
mice (BALB/c) rejecting the intrahepatic rat (Lewis) islet xenografts were
isolated and examined by two-color FACS analysis. RESULTS: The
characteristic finding of the hepatic MNC from the mice rejecting islet
xenografts compared with mice receiving isografts was a significant
increase in the yield as well as in the percentage of the cells expressing
CD3+ interleukin-2 receptor (IL-2R) alpha- beta+, CD3+ CD8alpha+ beta+,
and T cell receptor (TCR) alphabeta+ lymphocyte function-associated
antigen-1+. The expression of CD3 and TCR alphabeta of these T cells was
found to be of intermediate intensity (TCR(int) cells). The expansion of
these TCR(int) cells occurred predominantly in the liver. There was no

significant difference in the cells expressing CD3+ IL-2R alpha+, CD3+ CD4+, CD3+ TCRgammadelta+, CD3- IL-2Rbeta+ (natural killer cells), and B220+ (B cells). In vivo administration of anti-IL-2Rbeta **monoclonal antibody** directed to the expanded cells produced a prevention of rejection. CONCLUSIONS: These findings suggest that islet xenograft rejection in the liver from rat to mouse is an event for which the TCR(int) cells are responsible.

CT Check Tags: Animal; Support, Non-U.S. Gov't

Antibodies, Monoclonal: TU, therapeutic use
 Antigens, CD3: BI, biosynthesis
 Flow Cytometry
 Graft Rejection: PC, prevention & control
 Graft Survival: DE, drug effects
***Islets of Langerhans Transplantation: IM, immunology**
 Leukocytes, Mononuclear: CY, cytology
 *Liver: CH, chemistry
 Liver: CY, cytology
 Liver: SU, surgery
***Lymphocyte Function-Associated Antigen-1: AN, analysis**
 Mice
 Mice, Inbred BALB C
 Monocytes: CY, cytology
 Rats
 Rats, Inbred Lew
 *Receptors, Antigen, T-Cell, alpha-beta: AN, analysis
 *Receptors, Interleukin-2: IM, immunology
 Spleen: CY, cytology
 T-Lymphocytes: CY, cytology
 Thymus Gland: CY, cytology

***Transplantation, Heterologous: IM, immunology**
 CN 0 (**Antibodies, Monoclonal**); 0 (Antigens, CD3); 0
 (Lymphocyte Function-Associated Antigen-1); 0 (Receptors, Antigen, T-Cell,
 alpha-beta); 0 (Receptors, Interleukin-2)

L34 ANSWER 4 OF 17 MEDLINE

AN 95363081 MEDLINE

DN 95363081 PubMed ID: 7543517

TI Ex vivo coating of islet cell allografts with murine CTLA4/**Fc**
 promotes graft tolerance.

AU Steurer W; Nickerson P W; Steele A W; Steiger J; Zheng X X; Strom T B

CS Harvard Medical School, Department of Medicine, Boston, MA, USA.

SO JOURNAL OF IMMUNOLOGY, (1995 Aug 1) 155 (3) 1165-74.

Journal code: 2985117R. ISSN: 0022-1767.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199509

ED Entered STN: 19950921

Last Updated on STN: 19960129

Entered Medline: 19950912

AB To test the hypothesis that blockade of B7-triggered costimulation by donor cells could preclude allograft rejection, we coated crude islet allograft preparations in vitro for 1 h with a murine CTLA4/**Fc** fusion protein. Murine CTLA4/**Fc** blocks the proliferative response in primary mixed lymphocyte cultures (MLC) and Con A-stimulated murine spleen cell cultures by 85 to 95%. Responder cells from a primary MLC containing mCTLA4/**Fc** were hyporesponsive upon restimulation to the same stimulator cells in a secondary MLC lacking mCTLA4/**Fc**. Because of mutations in the **Fc** gamma RI and C'1q binding sites of the **Fc** portion of the murine CTLA4/**Fc** fusion protein, the molecule binds to, but does not target, cells for Ab-dependent cellular cytotoxicity or complement-directed cytotoxicity.

Although systemic immunosuppression was not applied, 42% (10 of 24) of B6AF1 recipients of islet allografts pretreated with CTLA4/**Fc** were permanently engrafted. Further, 50% of hosts bearing functioning islet allografts more than 150 days post-transplant were formally proved to be tolerant to donor tissues. A persistent CD4+ and CD8+ T cell infiltrate surrounding, but not invading, islet grafts in tolerant hosts was discerned. In control experiments, 89% (8 of 9) of islet allografts coated with mIgG3, and 100% (n = 10) pretreated with media alone were rejected. Thus, we conclude that 1) B7-triggered costimulation by donor APCs is an important element of rejection, and 2) blockade of the B7 pathway by in vitro allograft manipulation is able to induce tolerance.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Antigen-Presenting Cells: IM, immunology
 Antigens, CD28: IM, immunology
 Antigens, CD80: PH, physiology
 Antigens, Differentiation: GE, genetics
 *Antigens, Differentiation: PD, pharmacology

CHO Cells

Cell Line

Concanavalin A: PD, pharmacology

*Graft Enhancement, Immunologic

Graft Rejection: PC, prevention & control

Graft Survival: DE, drug effects

Graft Survival: IM, immunology

Hamsters

Immune Tolerance

Immunoglobulins, Fc: GE, genetics

*Immunoglobulins, Fc: PD, pharmacology

*Islets of Langerhans Transplantation

Lymphocyte Culture Test, Mixed

Lymphocyte Transformation: DE, drug effects

Mice

Mice, Inbred Strains

Mutagenesis, Site-Directed

Receptors, IgG: ME, metabolism

*Recombinant Fusion Proteins: PD, pharmacology

RN 11028-71-0 (Concanavalin A)

CN 0 (Antigens, CD28); 0 (Antigens, CD80); 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (Immunoglobulins, **Fc**); 0 (Receptors, IgG); 0 (Recombinant Fusion Proteins)

L34 ANSWER 5 OF 17 MEDLINE

AN 95350844 MEDLINE

DN 95350844 PubMed ID: 7624946

TI Prolongation of rat islet allograft survival by treatment with **monoclonal antibodies** against VLA-4 and LFA-1.

AU Yang H; Issekutz T B; Wright J R Jr

CS Department of Pathology, Izaak Walton Killam Children's Hospital, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, Canada.

SO TRANSPLANTATION, (1995 Jul 15) 60 (1) 71-6.

Journal code: 0132144. ISSN: 0041-1337.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199508

ED Entered STN: 19950911

Last Updated on STN: 19950911

Entered Medline: 19950831

AB In this study, we investigated the effects of treatment with

monoclonal antibodies against the VLA-4 and LFA-1

adhesion molecules on rat islet allograft rejection. TA-2 and TA-3 are

function-blocking **mAb** against rat VLA-4 and LFA-1, respectively. Lewis rats were made diabetic (plasma glucose levels > 22.2 mmol/L) with streptozotocin. One week later, 1500 freshly isolated Wistar Furth rat islets were transplanted under the left kidney capsule of each rat.

Monoclonal antibodies were administered intravenously at a dosage of 2 mg on the day of islet transplantation and then intraperitoneally every second day for 3 weeks or until graft rejection. Plasma glucose levels were monitored at least 3 times a week and blood leukocyte counts were monitored every 4 days. Rejection was defined as 2 plasma glucose levels > 11.1 mmol/L. Mean graft survival times in untreated and control **mAb**-treated rats were 5.3 and 6.0 days, respectively. Treatment with anti-VLA-4 or anti-LFA-1 resulted in only modest prolongation of mean graft survival time (9.3 and 7.4 days, respectively). However, treatment with the combination of anti-VLA-4 plus anti-LFA-1 resulted in long-term (i.e., 60-day) graft survival in 5 of 7 rats. Graft nephrectomy and histology confirmed islet graft survival at 60 days. A second Wistar Furth rat islet graft under the opposite renal capsule after graft nephrectomy did not show full tolerance; however, the function of the second graft was significantly prolonged without any immunosuppression. Combined blockade of VLA-4 and LFA-1 also markedly prolonged islet graft survival when islets were transplanted via the portal vein. In conclusion, both VLA-4 and LFA-1 play a role in islet allograft rejection and blockade of both prevents or greatly delays graft rejection.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't

***Antibodies, Monoclonal: TU, therapeutic use**

Diabetes Mellitus, Experimental: SU, surgery

Graft Rejection: PC, prevention & control

*Graft Survival: DE, drug effects

Islets of Langerhans: PA, pathology

***Islets of Langerhans Transplantation**

***Lymphocyte Function-Associated Antigen-1: IM, immunology**

Rats

Rats, Inbred Lew

Rats, Wistar

***Receptors, Very Late Antigen: IM, immunology**

Transplantation, Homologous

CN 0 (**Antibodies, Monoclonal**); 0 (Lymphocyte

Function-Associated Antigen-1); 0 (Receptors, Very Late Antigen)

L34 ANSWER 6 OF 17 MEDLINE

AN **95184773** MEDLINE

DN **95184773** PubMed ID: 7879120

TI Multilayer coating of **islets of Langerhans**: in vitro studies on a new method for immunoisolation.

AU Tatarkiewicz K; Sitarek E; Sabat M; Orłowski T

CS Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw.

SO TRANSPLANTATION PROCEEDINGS, (1995 Feb) 27 (1) 617.

Journal code: 0243532. ISSN: 0041-1345.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199504

ED Entered STN: 19950419

Last Updated on STN: 19950419

Entered Medline: 19950405

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Capsules

*Cell Separation: MT, methods

Cell Survival

Cells, Cultured

Centrifugation, Zonal: MT, methods
Heparin
***Islets of Langerhans: CY, cytology**
Islets of Langerhans Transplantation
 Protamines
 Rats

Transplantation, Heterologous

RN **9005-49-6 (Heparin)**

CN 0 (Capsules); 0 (Protamines)

L34 ANSWER 7 OF 17 MEDLINE

AN **95184663** MEDLINE

DN **95184663** PubMed ID: **7879025**

TI Potent immunosuppressive effect of anti-LFA-1 **monoclonal antibody** on islet allograft rejection.

AU Nishihara M; Gotoh M; Fukuzaki T; Ohta Y; Monden M; Yagita H; Okumura K; Miyasaka M; Mori T

CS Department of Surgery II, Osaka University Medical School, Japan.

SO TRANSPLANTATION PROCEEDINGS, (1995 Feb) 27 (1) 372.

Journal code: 0243532. ISSN: 0041-1345.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199504

ED Entered STN: 19950419

Last Updated on STN: 19950419

Entered Medline: 19950405

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't

***Antibodies, Monoclonal: TU, therapeutic use**

Blood Glucose: ME, metabolism

Diabetes Mellitus, Experimental: BL, blood

Diabetes Mellitus, Experimental: TH, therapy

*Graft Rejection: PC, prevention & control

Graft Rejection: TH, therapy

Hyperglycemia

*Immunosuppressive Agents: TU, therapeutic use

***Islets of Langerhans Transplantation: IM, immunology**

Islets of Langerhans Transplantation: PH, physiology

***Lymphocyte Function-Associated Antigen-1: IM, immunology**

Mice

Mice, Inbred BALB C

Mice, Inbred C57BL

Rats

Transplantation, Homologous

CN 0 (**Antibodies, Monoclonal**); 0 (Blood Glucose); 0

(Immunosuppressive Agents); 0 (Lymphocyte Function-Associated Antigen-1)

L34 ANSWER 8 OF 17 MEDLINE

AN **95134104** MEDLINE

DN **95134104** PubMed ID: **7832654**

TI In vitro and in vivo evaluation of protamine-heparin membrane for microencapsulation of rat **Langerhans islets**.

AU Tatarkiewicz K; Sitarek E; Fiedor P; Sabat M; Orłowski T

CS Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw.

SO ARTIFICIAL ORGANS, (1994 Oct) 18 (10) 736-9.

Journal code: 7802778. ISSN: 0160-564X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199502

ED Entered STN: 19950307
 Last Updated on STN: 19950307
 Entered Medline: 19950223

AB Rat **pancreatic islets** were microencapsulated with multilayer protamine-**heparin** (PH) membrane. Basal and stimulatory insulin secretion of microencapsulated **islets** was similar to the controlled free **islets** in vitro. During the long-term culture (up to 2 weeks) mean insulin release of encapsulated **islets** did not significantly differ from the mean of free ones (the ratio of mentioned means was 54-167%). Empty PH microcapsules transplanted into Wistar rats intraperitoneally and under the kidney capsule were generally harmless up to 4 months. In only a few cases traces of fibrotic tissue around capsules entrapped in the omentum were found. No damage of microcapsules structure was observed. The worst results were obtained in the instance of retroperitoneal transplantation. We conclude, therefore, that PH membrane was proved to be highly biocompatible, nontoxic for **islets**, and did not impair viability and glucose-dependent insulin secretion of **Langerhans islets** in in vitro culture.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
 Biocompatible Materials
 Cells, Cultured
Heparin
 Insulin: SE, secretion
Islets of Langerhans: CY, cytology
Islets of Langerhans: SE, secretion
***Islets of Langerhans Transplantation**
 *Membranes, Artificial
 Protamines
 Rats
 Rats, Wistar

RN 11061-68-0 (Insulin); **9005-49-6 (Heparin)**
 CN 0 (Biocompatible Materials); 0 (Protamines)

L34 ANSWER 9 OF 17 MEDLINE
 AN **95121104** MEDLINE
 DN **95121104** PubMed ID: **7821120**
 TI Immunomodulation of transplant rejection using **monoclonal antibodies** and soluble receptors.
 AU Alegre M L; Lenschow D J; Bluestone J A
 CS Department of Pathology, University of Chicago, Illinois 60637.
 SO DIGESTIVE DISEASES AND SCIENCES, (**1995 Jan**) 40 (1) 58-64. Ref: 40
 Journal code: 7902782. ISSN: 0163-2116.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, ACADEMIC)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199502
 ED Entered STN: 19950223
 Last Updated on STN: 19950223
 Entered Medline: 19950214

AB The main objective of our studies has been to optimize the effects of **monoclonal antibodies (MAbs)** and other immunosuppressive reagents to enhance organ graft survival. One such agent is OKT3, a **Mab** that is directed against the CD3 component of the human T-cell receptor (TCR) complex. Treatment of a rejection episode with OKT3 results in a rapid and efficient clearing of circulating T cells and reversal of most rejection episodes. Its wider use in transplantation and in the treatment of immune-mediated disease is limited by adverse reactions that follow the initial dose, the production of neutralizing

Abs, and the transient nature of the immunosuppression. We have engineered CDR-grafted "humanized" anti-CD3 **MABs** that lack **Fc** -receptor binding activity through mutagenesis of amino acids in the **Fc** portion of the **MAB**. This results in an immunosuppressive anti-CD3 **MAB** that is less antigenic and one that does not induce the first-dose side effects. In addition, we have pursued a goal of developing a therapy that will induce donor-specific tolerance while maintaining overall recipient immune competency. Because antigen-specific T-cell activation depends not only on TCR-ligand interaction, but also on additional costimulatory signals mediated by accessory molecules such as CD28, blocking the binding of CD28 on T cells to its ligand B7, during TCR engagement, might modulate transplantation responses. Using a soluble fusion protein of human CTLA4, CTLA4-Ig, that binds B7 with high affinity, inhibition of human **pancreatic islet** rejection that occurs, at least in part, by affecting T-cell recognition of human B7+ antigen-presenting cells has been demonstrated. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Human

Antibodies, Monoclonal: IM, immunology

***Antibodies, Monoclonal: TU, therapeutic use**

Graft Rejection: IM, immunology

*Graft Rejection: TH, therapy

*Immunosuppressive Agents: TU, therapeutic use

***Liver Transplantation**

Muromonab-CD3: TU, therapeutic use

*Receptors, Antigen, T-Cell: ME, metabolism

CN 0 (**Antibodies, Monoclonal**); 0 (Immunosuppressive Agents); 0 (Muromonab-CD3); 0 (Receptors, Antigen, T-Cell)

L34 ANSWER 10 OF 17 MEDLINE

AN 95090878 MEDLINE

DN 95090878 PubMed ID: 7998252

TI Protamine-heparin membrane for cell microencapsulation.

AU Tatarkiewicz K; Sitarek E; Fiedor P; Sabat M; Orłowski T

CS Institute of Biocybernetics and Biomedical Engineering, Warsaw, Poland.

SO TRANSPLANTATION PROCEEDINGS, (1994 Dec) 26 (6) 3509.

Journal code: 0243532. ISSN: 0041-1345.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199501

ED Entered STN: 19950126

Last Updated on STN: 19950126

Entered Medline: 19950118

CT Check Tags: Animal; Support, Non-U.S. Gov't

Blood Glucose: ME, metabolism

Capsules

Cell Survival

***Cell Transplantation: MT, methods**

Cells, Cultured

Diabetes Mellitus, Experimental: BL, blood

*Diabetes Mellitus, Experimental: TH, therapy

Glucose: PD, pharmacology

Graft Rejection

Heparin

***Islets of Langerhans: CY, cytology**

Islets of Langerhans: DE, drug effects

Islets of Langerhans: SE, secretion

***Islets of Langerhans Transplantation: MT, methods**

Islets of Langerhans Transplantation: PH, physiology

Mice

Mice, Inbred BALB C

Polyethyleneimine
 Protamines
 Rats
 Rats, Wistar
 *Transplantation, Heterologous: MT, methods
 Transplantation, Heterologous: PH, physiology
 RN 50-99-7 (Glucose); 9002-98-6 (Polyethyleneimine); 9005-49-6
 (Heparin)
 CN 0 (Blood Glucose); 0 (Capsules); 0 (Protamines); 0 (protamine-
 heparin membrane)

L34 ANSWER 11 OF 17 MEDLINE
 AN 95090770 MEDLINE
 DN 95090770 PubMed ID: 7998156
 TI Treatment with anti-VLA-4 and LFA-1 monoclonal
 antibodies prolongs intraportal rat islet allograft survival.
 AU Yang H; Issekutz T B; Wright J R Jr
 CS Department of Pathology, Izaak Walton Killam Children's Hospital, Halifax,
 Nova Scotia, Canada.
 SO TRANSPLANTATION PROCEEDINGS, (1994 Dec) 26 (6) 3325-6.
 Journal code: 0243532. ISSN: 0041-1345.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199501
 ED Entered STN: 19950126
 Last Updated on STN: 19950126
 Entered Medline: 19950118
 CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
 *Antibodies, Monoclonal: PD, pharmacology
 Diabetes Mellitus, Experimental: PA, pathology
 *Diabetes Mellitus, Experimental: TH, therapy
 *Graft Survival: PH, physiology
 Immunosuppression: MT, methods
 Islets of Langerhans Transplantation: IM, immunology
 Islets of Langerhans Transplantation: PA, pathology
 *Islets of Langerhans Transplantation: PH, physiology
 *Lymphocyte Function-Associated Antigen-1: IM, immunology
 Portal System
 Rats
 Rats, Inbred Lew
 Rats, Inbred WF
 *Receptors, Very Late Antigen: IM, immunology
 Transplantation, Heterotopic
 Transplantation, Homologous
 CN 0 (Antibodies, Monoclonal); 0 (Lymphocyte
 Function-Associated Antigen-1); 0 (Receptors, Very Late Antigen)

L34 ANSWER 12 OF 17 MEDLINE
 AN 94225606 MEDLINE
 DN 94225606 PubMed ID: 8171670
 TI Successful rat-to-mouse xenotransplantation of Langerhans
 islets microencapsulated within a protamine-heparin
 membrane.
 AU Tatarkiewicz K; Sitarek E; Fiedor P; Sabat M; Morzycka-Michalik M;
 Orłowski T
 CS Institute of Biocybernetics and Biomedical Engineering, Polish Academy of
 Sciences, Warsaw.
 SO TRANSPLANTATION PROCEEDINGS, (1994 Apr) 26 (2) 807-8.
 Journal code: 0243532. ISSN: 0041-1345.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)

LA English
 FS Priority Journals
 EM 199406
 ED Entered STN: 19940613
 Last Updated on STN: 19970203
 Entered Medline: 19940602
 CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
 Alginates
 Biocompatible Materials
 Biological Markers: BL, blood
 Blood Glucose: ME, metabolism
 Capsules
 Diabetes Mellitus, Experimental: BL, blood
 *Diabetes Mellitus, Experimental: SU, surgery
 Graft Rejection: DI, diagnosis
 *Graft Rejection: IM, immunology
 Heparin
 Islets of Langerhans Transplantation: IM, immunology
 ***Islets of Langerhans Transplantation: MT, methods**
 Mice
 Mice, Inbred BALB C
 Polyethyleneimine
 Polylysine: AA, analogs & derivatives
 Protamines
 Rats
 Rats, Wistar
 Transplantation, Heterologous: IM, immunology
 ***Transplantation, Heterologous: MT, methods**
 RN 25104-18-1 (Polylysine); 9002-98-6 (Polyethyleneimine); 9005-49-6
 (Heparin)
 CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Biological Markers); 0
 (Blood Glucose); 0 (Capsules); 0 (Protamines); 0 (alginate-polylysine-
 alginate); 0 (protamine-**heparin** membrane)

 L34 ANSWER 13 OF 17 MEDLINE
 AN **94225596** MEDLINE
 DN **94225596** PubMed ID: **7513474**
 TI Possible relationship between fibrotic overgrowth of alginate-polylysine-
 alginate microencapsulated **pancreatic islets** and the
 microcapsule integrity.
 AU de Vos P; Wolters G H; van Schilfgaarde R
 CS Surgical Research Laboratory, University of Groningen, The Netherlands.
 SO TRANSPLANTATION PROCEEDINGS, (1994 Apr) 26 (2) 782-3.
 Journal code: 0243532. ISSN: 0041-1345.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199406
 ED Entered STN: 19940613
 Last Updated on STN: 19970203
 Entered Medline: 19940602
 CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
 *Alginates
 Biocompatible Materials
 Capsules
 Dextrans
 Fibrosis
 ***Islets of Langerhans Transplantation: MT, methods**
 ***Islets of Langerhans Transplantation: PA, pathology**
 Membranes, Artificial
 *Polylysine: AA, analogs & derivatives
 Transplantation, Heterologous

Transplantation, Homologous

RN 25104-18-1 (Polylysine); 9004-54-0 (Dextrans); 9014-76-0 (sephadex)
 CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Capsules); 0
 (alginate-polylysine-alginate)

L34 ANSWER 14 OF 17 MEDLINE

AN **94025055** MEDLINE

DN **94025055** PubMed ID: **8212148**

TI Human **islet** isolation--a prospective randomized comparison of
pancreatic vascular perfusion with hyperosmolar citrate or
 University of Wisconsin solution.

AU Robertson G S; Chadwick D; Thirdborough S; Swift S; Davies J; James R;
 Bell P R; London N J

CS Department of Surgery, Leicester Royal Infirmary, United Kingdom.

SO TRANSPLANTATION, (1993 Sep) 56 (3) 550-3.

Journal code: 0132144. ISSN: 0041-1337.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199310

ED Entered STN: 19940117

Last Updated on STN: 19970203

Entered Medline: 19931028

AB University of Wisconsin solution has become the most commonly used
 vascular perfusate during multiorgan donation world-wide. In the UK
 however, hyperosmolar citrate remains in common use. The purpose of this
 prospective randomized study was to compare the effect of systemic
 perfusion with UW or HOC on subsequent **islet** yield and
 purification for **pancreata** with short cold ischemic times. Seven
pancreata were randomized to each group, with the donor age,
pancreas weight, and period of cold ischemia being similar in
 both. Perfusion with UW was shown to inhibit collagenase digestion, and a
 higher concentration of this enzyme was needed to achieve comparable
 numbers of **islets** with good separation of exocrine and
islet tissue after a similar period of digestion. There were no
 differences in the number, size, purity, or viability of **islets**
 between the two groups. In conclusion, UW solution offers no benefits over
 HOC for **pancreata** with short cold ischemic times, and because of
 its expense and need to use greater amounts of collagenase enzyme, we
 continue to use HOC.

CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't

Adenosine

Allopurinol

Cell Survival

Citrates: CH, chemistry

Citric Acid

Cold: AE, adverse effects

Collagenases: ME, metabolism

Glutathione

Insulin

Ischemia: ET, etiology

***Islets of Langerhans**

Islets of Langerhans: CY, cytology

Osmolar Concentration

*Pancreas: BS, blood supply

Perfusion

Prospective Studies


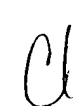
Raffinose

Random Allocation

Tissue Donors

RN 11061-68-0 (Insulin); 315-30-0 (Allopurinol); 512-69-6 (Raffinose);
58-61-7 (Adenosine); 70-18-8 (Glutathione); 77-92-9 (Citric Acid)
CN 0 (Citrates); 0 (University of Wisconsin-lactobionate solution); EC
3.4.24.- (Collagenases)

L34 ANSWER 15 OF 17 MEDLINE
AN **93102412** MEDLINE
DN **93102412** PubMed ID: **1465972**
TI Xenograft acceptance by masking donor antigens.
AU Faustman D; Coe C
CS Immunobiology Laboratories, Massachusetts General Hospital East,
Charlestown 02129.
SO TRANSPLANTATION PROCEEDINGS, (1992 Dec) 24 (6) 2854-5.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
ED Entered STN: 19930205
Last Updated on STN: 19930205
Entered Medline: 19930115
CT Check Tags: Animal; Human
*Antigenic Modulation: IM, immunology
Graft Rejection: IM, immunology
*Graft Survival: IM, immunology
*Immunoglobulin Fragments: IM, immunology
*Islets of Langerhans Transplantation: IM, immunology
Kidney
*Major Histocompatibility Complex: IM, immunology
Mice
Pilot Projects
Receptors, Antigen, T-Cell: IM, immunology
Receptors, Fc: IM, immunology
*T-Lymphocytes, Cytotoxic: IM, immunology
*Tissue Donors
Transplantation, Heterologous
*Transplantation, Heterotopic: IM, immunology
CN 0 (Immunoglobulin Fragments); 0 (Receptors, Antigen, T-Cell); 0
(Receptors, Fc)

L34 ANSWER 16 OF 17 MEDLINE
AN **92358237** MEDLINE
DN **92358237** PubMed ID: **1323143**
TI Long-term survival of xenogeneic **pancreatic islet**
grafts induced by CTLA4lg.
CM Comment in: Science. 1992 Aug 7;257(5071):751
AU Lenschow D J; Zeng Y; Thistlethwaite J R; Montag A; Brady W; Gibson M G;
Linsley P S; Bluestone J A
CS Ben May Institute, University of Chicago, IL 60637.
NC AI29531 (NIAID)
R29 DK40092 (NIDDK)
SO SCIENCE, (1992 Aug 7) 257 (5071) 789-92. 
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199209
ED Entered STN: 19920925
Last Updated on STN: 19970203
Entered Medline: 19920908
AB Antigen-specific T cell activation depends on T cell receptor-ligand 

interaction and costimulatory signals generated when accessory molecules bind to their ligands, such as CD28 to the B7 (also called BB1) molecule. A soluble fusion protein of human CTLA-4 (a protein homologous to CD28) and the immunoglobulin (Ig) G1 Fc region (CTLA4lg) binds to human and murine B7 with high avidity and blocks T cell activation in vitro. CTLA4lg therapy blocked human **pancreatic islet** rejection in mice by directly affecting T cell recognition of B7+ antigen-presenting cells. In addition, CTLA4lg induced long-term, donor-specific tolerance, which may have applications to human organ transplantation.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Antibodies, Monoclonal: TU, therapeutic use

Antigens, Differentiation: IM, immunology

*Antigens, Differentiation: TU, therapeutic use

*Diabetes Mellitus, Experimental: SU, surgery

*Graft Survival: IM, immunology

Graft Survival: PH, physiology

Immunoglobulin G

Immunoglobulins, Fc

*Immunosuppressive Agents: TU, therapeutic use

***Islets of Langerhans Transplantation: IM, immunology**

Islets of Langerhans Transplantation: PH, physiology

Mice

Mice, Inbred Strains

Phosphates: AN, analysis

*Phosphates: ME, metabolism

Receptors, Cell Surface: IM, immunology

*Recombinant Fusion Proteins: TU, therapeutic use

Time Factors

***Transplantation, Heterologous: IM, immunology**

Transplantation, Heterologous: PH, physiology

Uranium: AN, analysis

*Uranium: ME, metabolism

RN 18433-48-2 (hydrogen uranyl phosphate); 7440-61-1 (Uranium)

CN 0 (**Antibodies, Monoclonal**); 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (Immunoglobulin G); 0 (Immunoglobulins, **Fc**); 0 (Immunosuppressive Agents); 0 (Phosphates); 0 (Receptors, Cell Surface); 0 (Recombinant Fusion Proteins)

L34 ANSWER 17 OF 17 MEDLINE

AN 91262652 MEDLINE

DN 91262652 PubMed ID: 1710828

TI Prevention of xenograft rejection by masking donor HLA class I antigens.

AU Faustman D; Coe C

CS Diabetes Unit, Massachusetts General Hospital, Harvard Medical School, Boston 02129.

SO SCIENCE, (1991 Jun 21) 252 (5013) 1700-2.

Journal code: 0404511. ISSN: 0036-8075.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199107

ED Entered STN: 19910802

Last Updated on STN: 19960129

Entered Medline: 19910716

AB Destruction of target cells by cytotoxic T lymphocytes requires the presence of HLA (human lymphocyte antigen) class I antigens on the target cells for adhesion as well as for triggering of the antigen-specific T cell receptor. Rejection of xenogeneic human **pancreatic islets** and liver was circumvented by masking, before transplantation, donor antigens with F(ab')₂ antibody fragments to HLA

class I or tissue-specific epitopes. This strategy eliminated the need for recipient immunosuppression and allowed **islet** xenograft survival beyond 200 days, as demonstrated functionally by C peptide secretion as well as by histology. These in vivo observations are consistent with the importance of donor HLA class I in eliciting graft rejection and have potential applicability to the successful transplantation of other HLA class I-bearing donor tissues.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't

Antibodies, Monoclonal: IM, immunology

Antigen-Antibody Complex

Antigens, CD: IM, immunology

Antigens, CD29

C-Peptide: BL, blood

*Graft Rejection

*Histocompatibility Antigens Class I: IM, immunology

Immunoglobulins, Fab: IM, immunology

***Islets of Langerhans: IM, immunology**

***Islets of Langerhans Transplantation: IM, immunology**

Mice

Mice, Inbred BALB C

*T-Lymphocytes: IM, immunology

Transplantation, Heterologous

CN 0 (**Antibodies, Monoclonal**); 0 (Antigen-Antibody Complex); 0 (Antigens, CD); 0 (Antigens, CD29); 0 (C-Peptide); 0 (Histocompatibility Antigens Class I); 0 (Immunoglobulins, Fab)

=> d all tot

L38 ANSWER 1 OF 11 MEDLINE

AN 2001136510 MEDLINE

DN 20544218 PubMed ID: 11095109

TI Isolated human islets trigger an instant blood mediated inflammatory reaction: implications for intraportal islet transplantation as a treatment for patients with type 1 diabetes.

AU Bennet W; Groth C G; Larsson R; Nilsson B; Korsgren O

CS Department of Transplantation Surgery, Karolinska Institute, Huddinge Hospital, Sweden.

SO UPSALA JOURNAL OF MEDICAL SCIENCES, (2000) 105 (2) 125-33. Ref: 24
Journal code: 0332203. ISSN: 0300-9734.

CY Sweden

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 200103

ED Entered STN: 20010404

Last Updated on STN: 20010404

Entered Medline: 20010301

AB **Islet** transplantation offers a logical means to treat insulin-dependent diabetes. However, for reasons poorly understood, the clinical results with **islet** transplantation have been vastly inferior to those obtained with whole organ **pancreas** transplantation. The conventional technique for transplanting isolated **islets** is by intraportal injection, with the **islets** being trapped in the liver. Human **islets** exposed to human blood triggered an "instant blood mediated inflammatory reaction", IBMIR, characterised by platelet consumption, and activation of the coagulation and complement systems. The **islets** became surrounded by clots and infiltrated with leukocytes, and there was evidence of **islet** damage as reflected in insulin dumping. When **heparin** and a complement inhibitor (SCRI), was added to the system, IBMIR was suppressed

and **islet** damage reduced. After intraportal pig-to-pig **islet** intraportal allotransplantation similar morphological changes was found, corroborating the in vitro findings. Thus, IBMIR inflicts a significant damage to human **islets** exposed to human blood and IBMIR will also, most likely, enhance the subsequent specific, cell mediated, rejection. Platelet and complement activation seem to be the most important factors in the pathogenesis of IBMIR. The results presented strongly suggest that IBMIR observed both in vitro and in vivo when isolated **islets** come in contact with blood could provide an explanation for the unsatisfactory results seen in clinical **islet** allotransplantation.

CT Check Tags: Human; Support, Non-U.S. Gov't

Blood Coagulation

Blood Platelets: PH, physiology

Complement Activation

*Diabetes Mellitus, Insulin-Dependent: TH, therapy

*Inflammation: ET, etiology

***Islets of Langerhans Transplantation**

Portal System

Transplantation, Homologous

L38 ANSWER 2 OF 11 MEDLINE

AN 2000216291 MEDLINE

DN 20216291 PubMed ID: 10755515

TI Damage to porcine **islets** of **Langerhans** after exposure to human blood in vitro, or after intraportal transplantation to cynomolgus monkeys: protective effects of sCR1 and **heparin**.

CM Comment in: Transplantation. 2000 Mar 15;69(5):708-9

AU Bennet W; Sundberg B; Lundgren T; Tibell A; Groth C G; Richards A; White D J; Elgue G; Larsson R; Nilsson B; Korsgren O

CS Department of Transplantation Surgery, Karolinska Institutet, Huddinge Hospital, Sweden.

SO TRANSPLANTATION, (2000 Mar 15) 69 (5) 711-9.

Journal code: 0132144. ISSN: 0041-1337.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200004

ED Entered STN: 20000427

Last Updated on STN: 20000427

Entered Medline: 20000419

AB BACKGROUND: Porcine **islets** offer an attractive alternative to human **islets** in clinical **islet** transplantation. The preferred method of **islet** transplantation is intra-portal injection into the liver. We have recently shown, both in vitro with human **islets** and in vivo with porcine **islets**, that **islets** exposed to allogeneic blood trigger an injurious inflammatory reaction characterized by activation of both coagulation and the complement systems. We have now tested whether a similar reaction is triggered when xenogeneic porcine **islets** are exposed to human blood in vitro and after intraportal transplantation into primates. Furthermore, we investigated the effect of inhibiting the complement and coagulation systems. METHOD: **Islets** isolated from adult and fetal porcine **pancreas** were perfused with fresh human blood in surface heparinized PVC tubings for 5-60 min. Blood cell counts and parameters related to coagulation and the complement system were analyzed, and **islets** were retrieved after the perfusion was examined by immunohistochemical method. **Heparin** and soluble complement receptor 1 (sCR1; TP10, 100 microg/ml) were added to the system in some experiments. Furthermore, adult porcine **islets** were transplanted intraportally into untreated and sCR1- (40 mg/kg BW i.v.) treated cynomolgus monkeys, and plasma insulin concentration was monitored during

60 min after transplantation. RESULTS: Porcine **islets** perfused with human blood triggered an immediate inflammatory reaction, characterized by a rapid consumption and activation of platelets, consumption of neutrophils and monocytes, activation of the coagulation and complement systems, and release of large amounts of insulin.

Islet morphologic analysis revealed damaged **islets** embedded in clots and infiltrated with CD11+ leukocytes. C3a and C5b-9 was deposited on the **islet** surface, but human immunoglobulin was not. Complement inhibition with sCR1 reduced insulin release significantly. Intraportal **islet** transplantation into untreated cynomolgus monkeys resulted in a marked and rapid increase in plasma insulin concentration indicative of **islet** damage. Pretreatment of the monkeys with sCR1 resulted in significantly less insulin release than in untreated control monkeys. CONCLUSION: Exposure of isolated xenogeneic **islets** of **Langerhans** to blood, both in vitro and in vivo, resulted in acute **islet** damage. Complement and platelets seem to have a central role in the reactions described. Strategies to efficiently inhibit these reactions will be crucial for clinical intraportal **islet** xenotransplantation to be successful.

CT Check Tags: Animal; Human; In Vitro; Support, Non-U.S. Gov't

*Blood Physiology

Immunohistochemistry: MT, methods

Injections

Insulin: SE, secretion

Islets of Langerhans: ME, metabolism

Islets of Langerhans: PA, pathology

Islets of Langerhans: SE, secretion

***Islets of Langerhans Transplantation: MT, methods**

Macaca fascicularis

Perfusion

Portal System

Staining and Labeling

Swine

***Transplantation, Heterologous**

RN 11061-68-0 (Insulin)

L38 ANSWER 3 OF 11 MEDLINE

AN 1999440905 MEDLINE

DN 99440905 PubMed ID: 10512353

TI Incompatibility between human blood and isolated **islets** of **Langerhans**: a finding with implications for clinical intraportal **islet** transplantation?.

AU Bennet W; Sundberg B; Groth C G; Brendel M D; Brandhorst D; Brandhorst H; Bretzel R G; Elgue G; Larsson R; Nilsson B; Korsgren O

CS Department of Transplantation Surgery, Karolinska Institutet, Huddinge Hospital, Sweden.. william.bennet@transpl.hs.sll.se

SO DIABETES, (1999 Oct) 48 (10) 1907-14.
Journal code: 0372763. ISSN: 0012-1797.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199910

ED Entered STN: 19991101

Last Updated on STN: 19991101

Entered Medline: 19991019

AB The remarkable difference in success rates between clinical **pancreas** transplantation and **islet** transplantation is poorly understood. Despite the same histocompatibility barrier and similar immunosuppressive treatments in both transplantation procedures, human intraportal **islet** transplantation has a much inferior success rate than does vascularized **pancreas** transplantation. Thus far, little attention has been directed to the possibility that **islets**

transplanted into the blood stream may elicit an injurious incompatibility reaction. We have tested this hypothesis in vitro with human **islets** and in vivo with porcine **islets**. Human **islets** were exposed to nonanticoagulated human ABO-compatible blood in surface-heparinized polyvinyl chloride tubing loops. **Heparin** and/or the soluble complement receptor 1 (sCR1) TP10 were tested as additives. Adult porcine **islets** were transplanted intraportally into pigs, and the liver was recovered after 60 min for immunohistochemical staining. Human **islets** induced a rapid consumption and activation of platelets. Neutrophils and monocytes were also consumed, and the coagulation and complement systems were activated. Upon histological examination, **islets** were found to be embedded in clots and infiltrated with CD11+ leukocytes. Furthermore, the cellular morphology was disrupted. When **heparin** and sCR1 were added to the blood, these events were avoided. Porcine **islets** retrieved in liver biopsies after intraportal **islet** allotransplantation showed a morphology similar to that of human **islets** perfused in vitro. Thus, exposure of isolated **islets** of **Langerhans** to allogenic blood resulted in significant damage to the **islets**, a finding that could explain the unsatisfactory clinical results obtained with intraportal **islet** transplantation. Because administration of **heparin** in combination with a soluble complement receptor abrogated these events, such treatment would presumably improve the outcome of clinical **islet** transplantation by reducing both initial **islet** loss and subsequent specific immune responses.

CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't Adult

*Blood: IM, immunology

Enzyme-Linked Immunosorbent Assay

*Inflammation: ET, etiology

Inflammation: IM, immunology

Insulin: ME, metabolism

***Islets of Langerhans**: IM, immunology

Islets of Langerhans: ME, metabolism

***Islets of Langerhans Transplantation**: AE, adverse effects

Islets of Langerhans Transplantation: IM, immunology

Leukocyte Count

Middle Age

Platelet Count

Portal Vein

Rabbits

Swine

RN 11061-68-0 (Insulin)

L38 ANSWER 4 OF 11 MEDLINE

AN 1999086674 MEDLINE

DN 99086674 PubMed ID: 9869850

TI Reversal of hyperglycemia in streptozotocin diabetic mice by xenotransplantation of microencapsulated rat islets.

AU Tatarkiewicz K; Sitarek E; Sabat M; Orlowski T

CS Institute of Biocybernetics & Biomedical Engineering, Warsaw, Poland.

SO ANNALS OF TRANSPLANTATION, (1997) 2 (2) 20-3.

Journal code: 9802544. ISSN: 1425-9524.

CY Poland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199902

ED Entered STN: 19990216

Last Updated on STN: 19990216

Entered Medline: 19990202

AB Rat **pancreatic islets** were immunoisolated within alginate capsules with additional polyethyleneimine-protamine-

heparin highly biocompatible membrane. Perifusion study in vitro demonstrated satisfactory similarities between the insulin release profiles of encapsulated and free **islets**. Concordant xenotransplantation of microencapsulated rat **islets** significantly prolonged mean time of restored normoglycemia (46 +/- 15 days) in streptozotocin-diabetic BALB/c mice recipients comparing to uncoated grafts (7 +/- 2 days).

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Alginates

Blood Glucose: ME, metabolism

*Diabetes Mellitus, Experimental: SU, surgery

Heparin

*Hyperglycemia: SU, surgery

***Islets of Langerhans Transplantation**

Mice

Mice, Inbred BALB C

Microspheres

*Pancreas, Artificial

Polyethyleneimine

Polymers

Protamines

Rats

***Transplantation, Heterologous**

RN 9002-98-6 (Polyethyleneimine); 9005-32-7 (alginic acid); 9005-49-6
(**Heparin**)

CN 0 (Alginates); 0 (Blood Glucose); 0 (Polymers); 0 (Protamines)

L38 ANSWER 5 OF 11 MEDLINE

AN 96257665 MEDLINE

DN 96257665 PubMed ID: 8658913

TI Unpurified islet cell transplantation in diabetic rats.

AU Nomura Y; Ito S; Ichikawa N; Meigata K; Kikuchi K; Ando Y; Watanabe K;
Degawa H; Beck Y; Tomikawa S; Nagao T; Uchida H

CS Department of Surgery and Organ Transplantation, University of Tokyo,
Japan.

SO TRANSPLANTATION PROCEEDINGS, (1996 Jun) 28 (3) 1849-50.

Journal code: 0243532. ISSN: 0041-1345.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199608

ED Entered STN: 19960808

Last Updated on STN: 19960808

Entered Medline: 19960801

CT Check Tags: Animal; Male

*Anticoagulants: PD, pharmacology

Antithrombin III: PD, pharmacology

*Blood Pressure: DE, drug effects

Diabetes Mellitus, Experimental: SU, surgery

Gabexate: PD, pharmacology

*Graft Survival: DE, drug effects

Heparin: PD, pharmacology

***Islets of Langerhans Transplantation: MT, methods**

Islets of Langerhans Transplantation: PH, physiology

Portal Vein: DE, drug effects

*Portal Vein: PH, physiology

Rats

Rats, Wistar

Transplantation, Isogeneic

RN 39492-01-8 (Gabexate); 9000-94-6 (Antithrombin III); 9005-49-6
(**Heparin**)

CN 0 (Anticoagulants)

L38 ANSWER 6 OF 11 MEDLINE
 AN 96024684 MEDLINE
 DN 96024684 PubMed ID: 7573524
 TI Selective binding of platelet factor 4 to regions of active angiogenesis in vivo.
 AU Hansell P; Maione T E; Borgstrom P
 CS La Jolla Institute for Experimental Medicine, California 92037, USA.
 SO AMERICAN JOURNAL OF PHYSIOLOGY, (1995 Sep) 269 (3 Pt 2) H829-36.
 Journal code: 0370511. ISSN: 0002-9513.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199511
 ED Entered STN: 19951227
 Last Updated on STN: 19951227
 Entered Medline: 19951102
 AB In a previous study we suggested that recombinant human platelet factor 4 (rhPF4) preferentially binds in vivo to regions of active angiogenesis/endothelial cell migration. To test this hypothesis, binding of fluorescently labeled rhPF4 to newly formed vessels was compared with that of the normal skin vasculature, using syngeneic **Langerhans islets** as inducers of angiogenesis. **Islets** were implanted in the dorsal skinfold chamber of the hamster, and the binding of rhPF4 was studied using intravital fluorescence microscopy. Intra-arterially injected rhPF4 labeled, with high intensity, the endothelium along newly formed vessels of the **islets** (1,632 +/- 617 microns labeled vessel length per **islet**), and only on rare occasions (1 +/- 2 sites per cm2 skinfold) were short (62 +/- 48 microns) intense-labeled sites found in the normal vasculature of the skinfold. **Heparin** could displace most of the label if injected within 10 min after the rhPF4 injection, but not 30 min after. In conclusion, rhPF4-preferentially binds to regions of active angiogenesis in vivo. On binding, rhPF4 is internalized as judged from a decreasing **heparin** sensitivity with time after rhPF4 injection. The infrequent rhPF4-labeling sites in the normal skin vasculature most likely represent regions of newly formed cells/migration, i.e., normal endothelial turnover, supporting our previous findings demonstrating that the occurrence of such regions is rare in the normal microvasculature. Furthermore, despite the previously demonstrated short half-life in plasma, systemically injected rhPF4 will target regions of angiogenesis with high affinity, thereby facilitating the antiangiogenic effect of PF4.
 CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
 Fluorescein-5-isothiocyanate
 Hamsters
 Heparin: PD, pharmacology
 Islets of Langerhans: BS, blood supply
 Islets of Langerhans Transplantation
 Mesocricetus
 Microscopy, Fluorescence
 *Neovascularization, Physiologic: PH, physiology
 *Platelet Factor 4: ME, metabolism
 Recombinant Proteins: ME, metabolism
 Skin: BS, blood supply
 Skin: SU, surgery
 RN 3326-32-7 (Fluorescein-5-isothiocyanate); 37270-94-3 (Platelet Factor 4);
 9005-49-6 (**Heparin**)
 CN 0 (Recombinant Proteins)
 L38 ANSWER 7 OF 11 MEDLINE
 AN 93091097 MEDLINE
 DN 93091097 PubMed ID: 1457692

TI Hybrid artificial **pancreas: islet** transplantation
inside membrane bioreactors.

AU Lombardi C P; Urso A; Careddu G; Ghirlanda G; Catapano G; Brisinda G;
Ceriati F; Bellantone R; Doglietto G B; Crucitti F

CS Chair of Surgical Pathology, Catholic University, Rome, Italy.

SO BIOMATERIALS, ARTIFICIAL CELLS, AND IMMOBILIZATION BIOTECHNOLOGY,
(1992) 20 (5) 1177-92.
Journal code: 9111988. ISSN: 1055-7172.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199301

ED Entered STN: 19930129
Last Updated on STN: 19930129
Entered Medline: 19930114

AB The use of **pancreatic islet** transplantation in
membrane bioreactors put in vascular circuits aims at resetting the
glucose homeostasis in diabetic or **pancreatectomized** patients,
avoiding immune host rejection. Our experience was carried out at
following stages: porcine **pancreas** explantation and enzymatic
separation of endocrine tissue from exocrine fraction by collagenase;
evaluation of **islet** functionality (culture tests); in vitro
tests of the **islets**-bioreactor system, to assess the metabolic
response to the glucose; in vivo evaluation to assay the haemodynamic
behaviour. The trials showed a good metabolic bioreactor functionality and
a decreasing incidence of coagulative problems.

CT Check Tags: Animal; Female
Glucose: ME, metabolism
Heparin
Insulin: SE, secretion
***Islets of Langerhans Transplantation: MT, methods**
Membranes, Artificial
Swine

RN 11061-68-0 (Insulin); 50-99-7 (Glucose); 9005-49-6 (Heparin)

L38 ANSWER 8 OF 11 MEDLINE

AN 92314603 MEDLINE

DN 92314603 PubMed ID: 1377558

TI Induction of angiogenesis by growth factors: relevance to
pancreatic islet transplantation.

AU Stagner J I; Samols E

CS Veterans Administration Medical Center, Louisville, KY.

SO EXS, (1992) 61 381-5.
Journal code: 9204529.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199208

ED Entered STN: 19920815
Last Updated on STN: 19960129
Entered Medline: 19920806

AB Biodegradable pellets releasing 20 ng/day of endothelial cell growth
factor alpha (alpha ECGF) or a- or b-fibroblast growth factor (FGF) and 90
micrograms/day of **heparin** were implanted beneath the renal
capsule in rats and dogs and the muscularis/serosal border of the pyloric
stomach in dogs to test for angiogenesis in a potential **pancreatic**
islet transplant site. These factors were also tested in vitro to
determine whether the capillary bed of the isolated **islet** could
be preserved. alpha ECGF was superior to a- or bFGF in promoting
endothelial cell growth and capillary formation in isolated **islets**
. Both a- or bFGF and alpha ECGF induced the development of a dense

capillary bed in the dog stomach, whereas in the kidney site alpha ECGF was more effective in the rat than was a- or bFGF. Priming the isolated **islet** as well as the transplant site prior to **islet** transplantation resulted in **islet** blood flow being established within 3 days in contrast to 7-14 days in controls.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Capillaries: DE, drug effects

Capillaries: PH, physiology

Cells, Cultured

Dipyridamole: PD, pharmacology

Dogs

*Endothelial Growth Factors: PD, pharmacology

*Fibroblast Growth Factor 1: PD, pharmacology

*Fibroblast Growth Factor 2: PD, pharmacology

***Islets of Langerhans: BS, blood supply**

***Islets of Langerhans Transplantation: PH, physiology**

*Neovascularization, Pathologic

Rats

Regional Blood Flow: DE, drug effects

Transplantation, Heterologous

RN 103107-01-3 (Fibroblast Growth Factor 2); 104781-85-3 (Fibroblast Growth Factor 1); 58-32-2 (Dipyridamole)

CN 0 (Endothelial Growth Factors)

L38 ANSWER 9 OF 11 MEDLINE

AN 92087504 MEDLINE

DN 92087504 PubMed ID: 1750208

TI [Stable reduction of endogenous insulin production in the body in experimental insulin-dependent diabetes].

Ustoichivoe vosstanovlenie produktsii endogennogo insulina v organizme pri eksperimental'nom insulinzavisimom diabete.

AU Kudriashov B A; Ul'ianov A M

SO VOPROSY MEDITSINSKOI KHIMII, (1991 Jul-Aug) 37 (4) 40-3.

Journal code: 0416601. ISSN: 0042-8809.

CY USSR

DT Journal; Article; (JOURNAL ARTICLE)

LA Russian

FS Priority Journals

EM 199201

ED Entered STN: 19920209

Last Updated on STN: 19920209

Entered Medline: 19920121

AB Implantation of beta-cells allogenic culture into animals with alloxan diabetes did not produce persistent positive effect. The implanted beta-cells lost their viability as a result of toxic effect of natural diabetogenic factor occurring in blood plasma during insulin-dependent diabetes. Long-term administration of **heparin** into these animals within first 90 days of the experiment enabled to avoid the negative phenomenon and to neutralize the diabetogenic factor activity. Under these conditions the implanted beta-cells effectively produced endogenous insulin and the symptoms of diabetes disappeared within 14 months.

CT Check Tags: Animal; Male

Alloxan: PD, pharmacology

Blood Glucose: AN, analysis

*Diabetes Mellitus, Experimental: ME, metabolism

English Abstract

*Insulin: BI, biosynthesis

Islets of Langerhans Transplantation

Pituitary Hormones: BL, blood

Rats

RN 11061-68-0 (Insulin); 50-71-5 (Alloxan)

CN 0 (Blood Glucose); 0 (Pituitary Hormones); 0 (diabetogenic protein)

L38 ANSWER 10 OF 11 MEDLINE
 AN 87044406 MEDLINE
 DN 87044406 PubMed ID: 2877528
 TI [Surgical experiences with segmental pancreatic transplantation in type I diabetes].
 Chirurgische Erfahrungen mit der segmentalen Pankreastreansplantation bei Typ I Diabetikern.
 AU Abendroth D; Illner W D; Land W
 SO ZEITSCHRIFT FUR EXPERIMENTELLE CHIRURGIE, TRANSPLANTATION, UND KUNSTLICHE ORGANE, (1986) 19 (4) 234-6.
 Journal code: 8302880. ISSN: 0232-7295.
 CY GERMANY, EAST: German Democratic Republic
 DT Journal; Article; (JOURNAL ARTICLE)
 LA German
 FS Priority Journals
 EM 198611
 ED Entered STN: 19900302
 Last Updated on STN: 19950206
 Entered Medline: 19861128
 CT Check Tags: Human
 Antibiotics: TU, therapeutic use
 *Diabetes Mellitus, Insulin-Dependent: TH, therapy
 Follow-Up Studies
 Heparin: TU, therapeutic use
 Insulin: TU, therapeutic use
 *Islets of Langerhans Transplantation
 Somatostatin: TU, therapeutic use
 RN 11061-68-0 (Insulin); 51110-01-1 (Somatostatin); 9005-49-6 (Heparin)
 CN 0 (Antibiotics)

L38 ANSWER 11 OF 11 MEDLINE
 AN 77044312 MEDLINE
 DN 77044312 PubMed ID: 791227
 TI Studies with the autotransplanted ovine pancreas: glucagon and insulin secretion.
 AU Arcus A C; Ellis M J; Kirk R D; Beaven D W; Donald R A; Hart D S; Holland G W; Redekopp C
 SO AUSTRALIAN JOURNAL OF BIOLOGICAL SCIENCES, (1976 Jul) 29 (3) 223-36.
 Journal code: 0370613. ISSN: 0004-9417.
 CY Australia
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 197612
 ED Entered STN: 19900313
 Last Updated on STN: 19900313
 Entered Medline: 19761223
 AB Basic studies on the secretion of glucagon and insulin by the ovine pancreatic autotransplant in the neck are described. Of the 17 transplants in the series none failed to secrete glucagon and only three failed to secrete insulin in detectable amounts. The longest surviving transplant actively secreted both hormones 3 years after transplantation and five other transplants were functional and the animals healthy after 16 months. Exocrine secretion disappears shortly after transplantation. Sodium butyrate and alanine each promoted the secretion of both hormones by the transplant. Glucagon failed to promote insulin secretion by the transplant, although it apparently stimulated the ovine in situ pancreas. The immediate (presumably direct) effect of insulin was to inhibit transplant glucagon secretion. Hypoglycaemia induced by peripheral insulin administration failed to stimulate glucagon secretion by the transplant,

although it did promote glucagon secretion by the ovine in situ pancreas. **Heparin** did not markedly suppress basal transplant secretion of either glucagon or insulin. Phasic response patterns occurred with both hormones during long butyrate perfusions, although first-phase responsiveness was not a constant feature. In one trial, first-phase responses fell off with repeated short butyrate infusions. Glucagon and insulin secretory patterns in response to butyrate were remarkably alike, suggesting a common mechanism. Loss of specific functions by the ovine pancreas after transplantation is discussed.

CT Check Tags: Animal; Female
 Arginine: PD, pharmacology
 Butyrates: PD, pharmacology
 Dose-Response Relationship, Drug
 Glucagon: PD, pharmacology
 *Glucagon: SE, secretion
 Heparin: PD, pharmacology
 Insulin: PD, pharmacology
 *Insulin: SE, secretion
 *Islets of Langerhans: SE, secretion
 *Pancreas Transplantation
 Secretory Rate: DE, drug effects
 *Sheep: PH, physiology
 Stimulation, Chemical
 Transplantation, Autologous
 RN 11061-68-0 (Insulin); 74-79-3 (Arginine); 9005-49-6 (Heparin);
 9007-92-5 (Glucagon)
 CN 0 (Butyrates)

=> d his

(FILE 'MEDLINE' ENTERED AT 13:06:20 ON 18 DEC 2002)

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          DEL HIS
          E ISLET/CT
          E E24+ALL
L1      4277 S E8+NT
          E ISLET/CT
          E E23+ALL
L2      22706 S E12+NT
          E TRANSPLANTATION/CT
          E E3+ALL
L3      256333 S E3+NT
L4      135197 S E45+NT OR E46+NT OR E47+NT OR 348+NT OR E49+NT
L5      4759 S L3,L4 AND L1,L2
L6      4759 S L1,L5
L7      5008 S ISLET(L) (LANGERHAN? OR PANCREA?) AND L3,L4
L8      5008 S L6,L7
L9      18 S L8 AND HEPARIN
L10     2 S L8 AND RGD
L11     4 S L8 AND (ARG OR ARGIN?) () (GLY OR GLYC?) () (ASP OR ASPART?)
L12     0 S L8 AND ARGINYLGLYCYLASPART?
L13     63 S L8 AND MAB
L14     269 S L8 AND MONOCLON?(L)ANTIBOD?
          E MONOCLONAL ANTIBODY/CT
          E E1+ALL
          E E2+ALL
L15     217 S L8 AND E8+NT
          E PLATELET INTEGRIN/CT
          E INTEGRIN/CT
L16     28 S L8 AND E3-E96
L17     2 S L8 AND E97-E142
          E E143+ALL
L18     34 S L8 AND E13+NT

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L19 27 S L8 AND FC?
E FC RECEPTOR/CT
E E4+ALL
E E2+ALL
L20 5 S L8 AND E13+NT
L21 1 S L8 AND THROMBIN(L)ANTITHROMBIN
L22 5 S L8 AND ANTICOAGUL?
E ANTICOAGULANT/CT
E E8+ALL
L23 31 S L8 AND E7+NT
L24 101 S L9-L11,L16-L23
L25 30 S L13,L14 AND L24
L26 101 S L24,L25
L27 74 S L26 AND PY<=1999
L28 27 S L27 NOT AB/FA
L29 72 S L27/ENG
L30 16 S L29/HUMAN
SEL DN AN 3 7 8 11-15
L31 8 S L30 AND E1-E24
L32 56 S L29 NOT L30
SEL DN AN 11 13 27 28 30 31 32 33 38
L33 9 S E25-E51
L34 17 S L31,L33 AND L1-L33

FILE 'MEDLINE' ENTERED AT 13:43:29 ON 18 DEC 2002

L35 12 S L9 NOT L34
L36 9 S L35 AND PY<=1999
SEL L35 DN AN 2 3
L37 2 S E52-E57 AND L35
L38 11 S L36,L37